930-175 Clinical Significance of Plasma levels of Adrenomedullin (AM) in Pulmonary Hypertension (PH)

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AM, a potent hypotensive peptide, was originally isolated from human pheochromocytoma. AM reduces the blood pressure and the pulmonary vascular resistance, and increases pulmonary blood flow. Recent reports showed that AM mRNA and AM receptor mRNA are highly expressed in the lungs, suggesting a role of AM in the pulmonary circulation. To determine the clinical significance of AM in PH, we investigated the relationship between plasma levels of AM and pulmonary hemodynamics in patients with PH. Venous blood samples were obtained during cardiac catheterization and plasma levels of AM were measured by specific radioimmunoassay in 20 consecutive patients with severe PH (8 primary, 12 chronic thromboembolic PH, M/F 10/10, 48 ± 15 yrs, mean pulmonary arterial pressure: 55 ± 14 mmHg). The plasma levels of AM were significantly higher in PH than in age-matched normal controls (PH: 10.3 ± 9.5, control: 5.1 ± 0.4 fmol/ml, $p < 0.05$), although there was no correlation with mean pulmonary arterial pressure taken as a whole. There were significant correlations between plasma levels of AM and mean right atrial pressure ($r = 0.74$, $p < 0.01$), stroke volume ($r = -0.63$, $p < 0.01$), total pulmonary resistance ($r = 0.64$, $p < 0.01$) and atrial natriuretic peptide ($r = 0.61$, $p < 0.01$). After the follow up of one year (mean 14 ± 4 months), the survival rate was significantly lower in patients with higher plasma levels of AM (> 10 fmol/ml) compared with those with lower AM (<10 fmol/ml) (28% versus 92%, $p < 0.01$). These results suggest that plasma levels of AM are elevated in severe PH and that they may reflect the right ventricular failure rather than the degree of PH. The plasma levels of AM may be a useful noninvasive biochemical marker of prognosis in severe PH.

930-176 Evaluation of Plasma Natriuretic Peptides (N-terminal proANP, cANP (99–126), proBNP (22–46), BNP-32, CNP-22) as Markers for Left Ventricular Dysfunction

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In patients with left ventricular (LV) dysfunction plasma levels of natriuretic peptides are increased correlating to the hemodynamic abnormalities and might, therefore, serve as indicators for LV dysfunction. We tested the hypothesis that N-terminal pro ANP (nANP) may be a more sensitive marker for LV dysfunction than other natriuretic peptides.

Plasma levels of atrial natriuretic peptide (99–126) (cANP), nANP (26–55), nANP (80–96), brain natriuretic peptide (BNP-32), proBNP (22–46) and C-type natriuretic peptide (CNP-22) were measured in 211 subjects before routine cardiac catheterization. The sensitivity and specificity of these hormones for LV dysfunction was evaluated by receiver operating characteristic analysis (ROC). In patients with LV ejection fraction (LVEF) ≤ 45% (n = 38) both nANPs, cANP (99–126), and BNP-32 were significantly increased. NANP was also elevated in patients with hypertension and normal LVEF. The correlation of nANP (80–96) to LVEF ($r = 0.55$, $p < 0.0001$), LV end-diastolic pressure ($r = 0.35$, $p < 0.0001$), right atrial and pulmonary artery pressure were superior to those of nANP (26–55), cANP (99–126) and BNP-32. There was no correlation between LVEF and proBNP (22–46) or CNP-22. The areas under ROC curves for LVEF ≤ 45% were 0.817 for nANP (80–96), 0.761 for nANP (22–56), 0.729 for cANP (99–126) and 0.683 for BNP-32 indicating high diagnostic accuracy, whereas the values for proBNP (0.515) and CNP-22 (0.525) suggested weak accuracies.

CANP (99–126), nANP (80–96), nANP (26–55) and BNP-32 are significantly correlated to hemodynamic variables indicating LV dysfunction with a superior sensitivity of nANP (80–96). However, due to the large scatter of normal values, plasma levels alone are of limited value as indicators of LV dysfunction in the individual patient.

930-177 Brain Natriuretic Peptide is a Marker of New York Heart Association Classification in Out-Patient Follow-Up of Left Ventricular Dysfunction

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New York Heart Association Classification (NYHA) and ejection fraction (EF) have prognostic implications in humans with left ventricular dysfunction (LVD). While brain (BNP), C- and N-terminal atrial (C-ANP, N-ANP) natriuretic peptides (NPs) are elevated in LVD, it is unclear which one best correlates with NYHA and if this relationship remains in out-patient follow-up. The correlation between NYHA class and the NPs and EF on Visit 1 and Follow-up were investigated within univariate (UV) and multivariate (MV) ordinal logistic models in 93 patients with LVD [NYHA I (17), II (36), III (27), IV (13)].

Visit 1:	UV	MV	Follow-up:	UV	MV
BNP	p = 0.0001	0.0001	BNP	0.0184	0.0432
C-ANP	0.0001	0.5638	C-ANP	0.0537	0.3810
N-ANP	0.0008	0.7187	N-ANP	0.0284	0.1312
EF	0.0001	0.0718	EF	0.1846	0.3629

At Visit 1, univariately BNP, C-ANP, N-ANP and EF were associated with NYHA class. Only BNP was independently associated with NYHA class in the multivariate model. BNP was also the most sensitive and specific marker for NYHA class as determined by the the area under the ROC curve. In the 42 follow-up visits, 23 patients had no change in NYHA class, 17 improved by one or more class and two deteriorated. Univariately, improved NYHA class was associated with decreases in BNP. Further, only BNP and not EF was an independent predictor within the multivariate model. These studies suggest that endogenous BNP may serve as a marker of NYHA class which may be useful in the objective assessment of functional class during the follow-up of patients with ventricular dysfunction.

930-178 The Natriuretic Peptides as Diagnostic Markers of Systolic Dysfunction – Comparison with a Simple Clinical Score

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There is growing interest in the use of C-terminal (C-ANP) and N-terminal (N-ANP) atrial and brain (BNP) natriuretic peptides as diagnostic markers of reduced ejection fraction (EF) which may allow screening of patients (pts) at risk without the high cost of echo. However, the predictive value of these markers must be compared to that of data available from a routine clinical evaluation including ECG and chest radiograph (CXR). To do this, we studied 304 consecutive out-pts referred for echo to evaluate EF because of symptoms of or risk factors for reduced EF. Blood was drawn at the time of echo. Clinical data was obtained from chart review. Clinical predictors of reduced EF in the 304 pts were examined and a score system (Score = 0–6) was developed focusing on simplicity, non-subjective nature of the data and predictive value. Patients received 1 point for each of the following: orthopnea or paroxysmal nocturnal dyspnea; history of heart failure; history of myocardial infarction; Q wave or intraventricular conduction defect on ECG; cardiothoracic ratio > 0.55 on CXR; venous congestion or edema on CXR. In this population, the prevalence of an EF < 45% was 12.5%. The sensitivity of a Score > 0 for predicting an EF < 45% was 100% with a specificity of 65%. At the same level of specificity, the sensitivity of a BNP > 40 pg/ml was 79%, a C-ANP > 47 pg/ml was 79% while a N-ANP > 911 pg/ml was 55%. In pts with a Score of 0 (n = 174), none had an EF < 45%. In pts with a Score > 0 (n = 130), 29% had an EF < 45%. *Conclusions:* While BNP or C-ANP may prove useful as diagnostic markers in some pts at risk, in this study of out-pts referred for echo to rule out systolic dysfunction, the predictive value of data available from the routine clinical evaluation was equivalent if not better. These data suggest that simple clinical data could be better used to limit the number of echos performed without sacrificing diagnostic accuracy for the detection of reduced EF.

931 Adult Cardiothoracic Surgery I

Monday, March 17, 1997, Noon–2:00 p.m.
Anaheim Convention Center, Hall E
Presentation Hour: 1:00 p.m.–2:00 p.m.

931-76 Using Prolonged Risk-Adjusted Post-Operative Length of Stay (RAPOLOS) to Measure Comparative Surgical Performance in CABG Procedures

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Difficulty differentiating among high quality cardiac surgical programs using risk-adjusted mortality rates has heightened interest in measuring rates of post-operative complications. However, inconsistent reporting of complications has undermined the usefulness of this measure. To create an objective criterion that can be applied uniformly, complications were identified by: (1) for each facility being evaluated, creating an XmR control chart for RAPOLOS

for CABG patients with no reported complications, (2) iteratively removing outliers until all cases are within 3 SD confidence limits, (3) classifying all patients discharged alive after prolonged RAPOLOS (based on the upper confidence limits of facilities' final XmR charts) as having had post-operative complications, and (4) computing risk-adjusted rates of adverse outcomes (death or prolonged RAPOLOS). To assess the ability of this method to discriminate among programs, data on inpatient mortality, complications, lengths of stay, and pre-operative patient characteristics required for risk adjustment were collected on 6,628 CABG procedures at 17 facilities. Mortality rates ranged from 0.8% to 4.9% (average 2.9%), but risk-adjusted mortality did not vary significantly among hospitals (χ^2 = 23.0). Upper confidence limits for RAPOLOS for patients classified as uncomplicated ranged from 6.1 to 9.7 days, indicating wide variations in practice patterns among hospitals. Of patients with no reported complications, an average of 4.0% had prolonged RAPOLOS (range 0–12%). Reported complication rates averaged 44.2% (range 27.0%–74.7%). Of patients with reported complications, 40.7% had prolonged RAPOLOS (range 23.4%–61.8%). Adverse outcome rates averaged 19.5% (range 11.4%–28.7%). Risk-adjusted adverse outcome rates ranged from 17.9% lower to 84.7% higher than predicted (χ^2 = 89.3, df = 16, P < 0.01) with 8 outlier facilities identified at the P < 0.05 level. *Conclusion:* Sensitive and objective measurements of comparative surgical performance can be achieved by combining standard methods of statistical process control and risk adjustment to identify prolongations in RAPOLOS beyond hospital-specific norms for CABG patients.

931-77 Quantitation of Myocardial F-18 Deoxyglucose Uptake Predicts Wall Motion Recovery After Revascularization

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To determine if quantitation of F-18 deoxyglucose (FDG) uptake identifies severely asynergic segments which recover wall motion (WM) after coronary revascularization (CABG), we studied 11 patients (pts) who underwent CABG after glucose loaded FDG PET scans. Myocardial uptake was measured with regions of interest in PET images acquired 40 to 60 minutes after 10 mCi (370 MBq) FDG and normalized to peak myocardial activity. Regional WM was scored from zero (normal) to 5 (dyskinetic) in pre and post CABG radionuclide ventriculograms by 3 blinded readers.

Six pts improved LVEF after CABG (0.32 ± 0.10 to 0.49 ± 0.11; p < 0.001); five patients did not (0.34 ± 0.11 to 0.31 ± 0.07). In the 10 severely asynergic segments which recovered WM (Group I), FDG uptake was significantly higher than in the 7 segments which did not improve (Group II). Despite technically successful revascularization, asynergic segments with preop FDG uptake less than 50% of peak myocardial activity failed to regain wall motion after CABG.

	Wall Motion Score				Preoperative FDG Uptake	
	n	Preop	Post Op	P-Value	Mean	Range
Group I	10	3.7 ± 0.7	1.5 ± 0.7	<0.001	0.69* ± 0.13	0.56–0.91
Group II	7	3.5 ± 0.6	3.7 ± 0.7	n.s.	0.38* ± 0.09	0.24–0.46

p * < 0.001

We conclude that functional recovery after CABG, can be predicted in severely asynergic segments when FDG uptake exceeds 50% of peak myocardial activity.

931-78 Minimally-Invasive Mitral Valve Surgery on Bypass with Cardioplegic Arrest

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In order to minimize surgical trauma minimally-invasive cardiac surgery has recently been started in patients with coronary artery disease. The aim of this study was to extend the application to mitral valve replacement or repair (MVR) using an endovascular cardiopulmonary bypass (CPB) system (Heartport Inc., Redwood City, CA, U.S.A). Between March and August 1996 nine patients (4 male, 5 female, age 47 to 69 years, median 64 years) underwent minimally-invasive MVR surgery. The underlying diseases were: mitral valve insufficiency (n = 3) and combined mitral valve disease (n = 6). Through a small right thoracotomy (6–8 cm) the pericardium was opened longitudinally. CPB was instituted through femoral cannulation and an intraaortic balloon-catheter was introduced for aortic occlusion, aortic root venting and delivery of cold antegrade crystalloid cardioplegia. Through a catheter inserted via the jugular vein, pulmonary artery venting was achieved. After incision of the left atrium, exposure of the mitral valve was accomplished using an atrial retractor. A mechanical prothesis was inserted and secured to the annulus with single pledged sutures in eight cases. In one case MV-repair was performed with insertion of an annuloplasty-ring. All patients were weaned from CPB either without or with low inotropic support. There was no perivalvular leak or residual mitral valve regurgitation found on intraoperative transesophageal echocardiography (TEE) in any patient. Time of ventilation, ICU- and hospital-stay were comparable with those of patients undergoing conventional MVR-surgery. In three patients TEE showed normal ventricular and prosthetic valve function at the two month follow up. Minimally-invasive MVR is feasible under the safety of CPB and cardioplegic arrest, avoiding sternotomy related complications thus resulting in earlier rehabilitation.

931-79 Protective Action of Aprotinin During Cardiopulmonary Bypass: Biochemical and Hemodynamic Effects

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We evaluated the protective role of aprotinin during standard cardiopulmonary bypass (CPB) in two groups of pigs (15–20 kg): Eight animals with 1 million KI units of aprotinin given before CPB (half prior to surgery and half before CPB) and ten animals in a control group. We instrumented the left ventricle with a high fidelity micromanometer and with two pairs of ultrasonic crystals to measure minor antero-posterior free wall and major base-apex diameters to approximate LV volume. After standard cannulation, steady state CPB was established for 45 min. Aortic cross clamp was applied for the first 30 min of CPB. Hemodynamic data were acquired during vena caval occlusion before and after CPB. We determined the slope (ESPVR, mmHg/ml) of the end-systolic pressure-volume relation, and the slope of the end-diastolic (EDPVR, mmHg/ml) pressure-volume relation. Blood samples for endothelial relaxation factor (EDRF/NO, uM) analysis and pO2 (mmHg) were taken before (*preCPB*) and immediately after CPB (*postCPB*). Results (median, paired t-test, *p < 0.05 between *preCPB* and *postCPB*, $^{+}$p < 0.05 between the groups):

	Control (n = 10)		Aprotinin (n = 8)	
	pre CPB	*post CPB*	*pre CPB*	*post CPB*
ESPVR	18.0	13.5*	17.9	22.0*
EDPVR	0.23	0.24	0.24	0.22
EDRF	0.18	0.16	0.31	0.28
pO_2	195	103*$^{+}$	227	147*$^{+}$

We conclude that aprotinin exibits protective hemodynamic action against damaging effects of CPB manifested in better LV systolic function post CPB. The mechanism of this action may be related to better oxygenation and an increased level of EDRF post CPB.

931-80 Troponin T Release during Reperfusion Predicts Delayed Recovery of Left Ventricular Function after CABG

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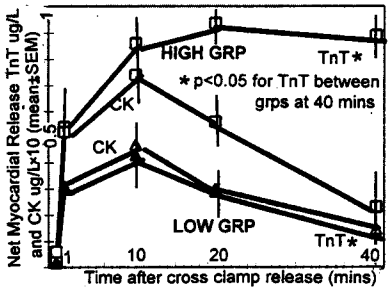
Myocardial damage sustained during ischemic arrest after CABG may be followed by further injury during reperfusion. We compared the release of troponin T (TnT), a bound cardiac protein with creatine kinase-MB(CK), a soluble cytosolic component during reperfusion as markers of injury to determine their influence on recovery of global LV function. *Method:* 14 pts undergoing CABG for 3 vessel disease with preserved LV function had coronary sinus and arterial blood samples obtained pre-cross clamp (CC), 1, 10, 20 and 40 mins after CC release for analysis of AV difference (AVD) of TnT and CK. Thermodilution cardiac output and high fidelity LV pressure measurements were made pre CC, 0.5, 1 and 3 hrs after CC release.



Results: In the HIGH TnT release grp (7 pts), negative AVD for TnT (net myocardial release) at 10 mins was > 0.5 μg/l compared to the LOW grp